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Hypernatremia Associated with Cathartics in Overdose Management

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ACTIVATED CHARCOAL has held a recognized role in acute poisoning management for more than 150 years.^{1,2} Its remarkable capacity to absorb chemicals has led to wide acceptance for the initial gastrointestinal decontamination.¹ Recent reports using multiple doses have shown increased systemic clearance for several drugs including phenobarbital,³ theophylline,⁴ digitoxin,⁵ carbamazepine⁶ and phenylbutazone.⁶ Multiple doses of activated charcoal also have been recommended for toxic ingestions of drugs that undergo enterohepatic circulation or gastric secretion (tricyclic antidepressants and phencyclidine).⁷ Although activated charcoal avidly absorbs toxins, binding is not irreversible.¹ Cathartic administration has therefore been recommended to hasten the elimination of the charcoal-toxin complex from the bowel and to prevent toxin desorption.⁸ The use of cathartics has also been advocated for preventing charcoal impaction when used in multiple doses.^{3,9}

Despite the wide use of cathartics, clear evidence of risk and benefit has not been described.¹ POISINDEX, a commonly used resource for poison management,⁷ recommends

for phencyclidine overdose that several doses of activated charcoal be administered every two to six hours with a cathartic until charcoal appears in the stool. A particular cathartic is not preferred but several precautions are mentioned:

- Doses should not be repeated if bowel sounds are absent.
- The fluid and electrolyte status should be monitored in a health care facility, especially in children.
- The safety of the repeated use of cathartics has not been established when used with multiple-dose charcoal regimens.
- In young children, cathartics should be administered no more than one to two times per day.

In a recent editorial on the rebirth of activated charcoal, Spyker said,

Although some cathartic is probably necessary to prevent formation of intestinal charcoal briquettes, we need to further assess quantitative importance of sorbitol and other cathartics. We must also assess the adverse effects of the cathartic on diarrhea and fluid and electrolyte management.¹⁰

Minocha and co-workers, after investigating the effects of single doses of 150 ml of 70% sorbitol, concluded that the possible effects of multiple-dose regimens and the effects in pediatric and geriatric populations need further study.¹¹ Case reports of hypernatremia associated with using cathartics are not found in the medical literature. Thus, the risks and benefits of multidose charcoal-cathartic combinations are inadequately defined.

We report three cases of severe hypernatremia associated with three different multidose charcoal-cathartic regimens during treatment of acute intoxication.

Reports of Cases

Case 1

The patient, a 22-year-old woman, was admitted to the emergency department with a presumptive overdose of amitriptyline and naproxen. She was initially lethargic but shortly became comatose. Her temperature was 37.2°C (99°F), pulse 108 per minute, respirations 26 per minute and blood pressure 120/70 mm of mercury. Her pupils were 4 mm, equal, round and sluggishly reactive to light. The abdomen was soft, bowel sounds were normally active and the skin was warm and dry. The results of the physical examination otherwise were normal. The electrocardiogram (ECG) showed a sinus rhythm with a PR interval of 0.20 seconds, a QRS duration of 0.12 seconds and a QT interval of 0.36 seconds. A chest x-ray film, leukocyte count and differential, hemoglobin and hematocrit were all normal. A blood alcohol level was 79 mg per dl. An endotracheal tube was inserted and gastric lavage done without return of pill fragments. She was then treated with a regimen of fluids given intravenously, 40% oxygen and 50 grams activated charcoal and 300 ml of a magnesium citrate solution (Citroma, National Magnesia Company, Glendale, NY) every four hours by nasogastric tube (Figure 1). A preparation of activated charcoal in a 70% sorbitol solution (Actidose charcoal solution, Paddock Laboratories, Inc, Minneapolis) was inadvertently administered. The initial serum sodium level two hours after admission was 138 mmol per liter. A solution of 5% dextrose and 0.45% saline was being administered at 75 ml per hour and the urine output was 150 ml per hour (Figure 1). Fluid administration 15 hours after admission was increased due to a decreasing urine output. The urine specific gravity had increased to 1.030. After 27 hours, the serum sodium concentration was

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noted to be 160 mmol per liter. Repeat determinations confirmed the presence of hypernatremia. The serum urea nitrogen level increased from 6.0 mg per dl on admission to 11 mg per dl, and the serum creatine level increased from 0.7 mg per dl to 1.3 mg per dl. The patient was still stuporous and large, watery, charcoal stools were noted. Fluid administration was increased again and changed to a 5% dextrose solution given intravenously and additional tap water through a nasogastric tube. The serum sodium level rose to 170 mmol per liter 34 hours after admission and then gradually declined with continued water replacement. Urine output, urine specific gravity and the serum sodium level had returned to normal 50 hours after admission. The patient was alert, oriented and taking oral feedings without diarrhea.

Case 2

The patient, a 34-year-old paraplegic woman, was admitted to the emergency department with an amitriptyline and barbiturate overdose. On admission she was combative but soon became lethargic and then comatose, requiring endotracheal intubation for respiratory support. Her pulse was 120 per minute and pupils were 3 mm and reactive to light, but sluggish to respond. The abdomen was flat with hypoactive bowel sounds, and deep tendon reflexes were equal with bilat-

eral Babinski's reflexes. The results of the physical examination were otherwise normal.

The ECG showed a heart rate of 150 per minute, a PR interval of 0.14 seconds, a QRS duration of 0.06 seconds, a QT interval of 0.28 seconds and peaked P waves. The hemoglobin was 10 grams per dl (100 grams per liter), the hematocrit was 31.3% (0.313) and the leukocyte count was 12,500 per μ l with a normal differential. Urinalysis showed a specific gravity of 1.010, 4+ protein, 50 to 100 leukocytes per high power field and 4+ bacteria. A urine Gram's stain showed 0 to 3 leukocytes, 5 to 10 gram-negative rods and 0 to 3 gram-positive cocci per oil immersion field. A chest x-ray film and results of a lumbar puncture were normal.

A gastric lavage was done, which did not yield evidence of pill fragments. Therapy was initiated with intravenous administration of fluids, nafcillin sodium and tobramycin given intravenously and 50 grams of activated charcoal and 150 ml of magnesium citrate every four hours through a nasogastric tube. The initial serum sodium level was 138 mmol per liter and a blood glucose level was 140 mg per dl (7.7 mmol per liter). A solution of 5% dextrose and 0.45% saline at 100 ml per hour was administered and the urine output was more than 180 ml per hour (Figure 1). Urine output 14 hours after admission decreased to less than 20 ml per hour with a urine specific gravity of 1.030. Her temperature was 40°C (104°F), respirations were 47 per minute and the blood pressure was 90/64 mm of mercury. The nursing staff noted black liquid stools too numerous to count. The patient removed the endotracheal tube herself nine hours after admission and was alert and oriented to person and place but not to time. Volume expansion with a normal saline solution was attempted, and the volume of maintenance fluids was increased to 300 ml per hour. Her serum sodium level 32 hours after admission was 164 mmol per liter—corrected to 175 mmol per liter due to hyperglycemia—and a blood glucose level was 698 mg per dl. The serum urea nitrogen concentration was increased to 27 and serum creatine to 2.9 mg per dl from initial values of 12 and 0.6 mg per dl, respectively. An insulin infusion was begun and intravenous fluids were changed to a solution of 0.45% sodium chloride.

Her serum sodium level 48 hours after admission had returned to normal, but urine output remained low and the patient continued to deteriorate clinically. A generalized paralytic ileus occurred 20 hours after admission and continued, accompanied by massive abdominal distention, rising ventilation pressures, mottling of the lower extremities and hypotension despite supportive measures. The patient died 58 hours after admission.

The autopsy showed massive thrombosis of the portal vein and a small bowel ileus. Gastric analysis showed acetaminophen, amitriptyline and an unidentified substance. A urine toxicology screen was positive for acetaminophen, amitriptyline and nortriptyline. A postmortem blood amitriptyline concentration was 1,151 ng per ml.

Case 3

The patient, a 37-year-old man, was found unresponsive by his brother. According to his friends, he had been drinking alcohol excessively and smoking phencyclidine (PCP). In the emergency department, he was obtunded, responsive to pain and occasionally combative. Superficial abrasions and contusions were noted on all four extremities. Except for nys-

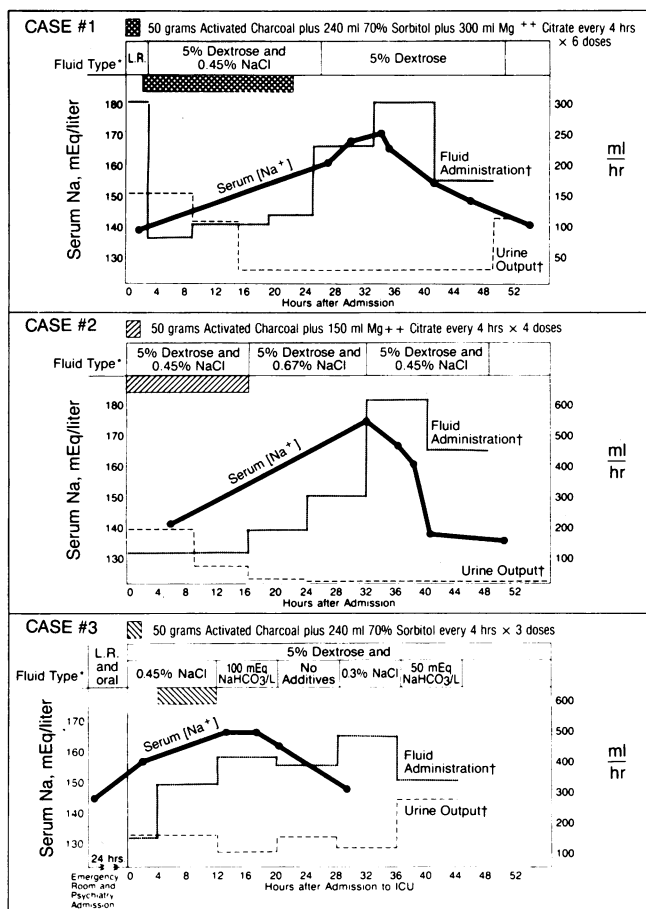


Figure 1.—The graph shows rising serum sodium concentrations accompanied by declining urine outputs despite the administration of fluids in excess of maintenance requirements in three patients who were administered multiple doses of cathartics and charcoal during overdose management.

*Most representative fluid type per time interval.

†Average ml/hr/6- to 8-hr time interval.

— = serum [Na⁺], = fluid administration, --- = urine output, ICU = intensive care unit, L.R. = lactated Ringer's solution

tagmus, the results of the physical examination were normal. He was treated with nasogastric intubation, gastric lavage and administration of 50 grams activated charcoal, 300 ml magnesium citrate solution and a lactated Ringer's solution given intravenously. A urine drug screen was positive for phencyclidine and nicotine. Arterial blood gas measurements, serum electrolytes, blood levels of glucose, urea nitrogen and alcohol, an ECG, urinalysis and cranial computed tomography were all normal.

During the eight-hour emergency department stay, he received 1,800 ml of fluid, 10 mg diazepam and 10 mg haloperidol given intramuscularly for agitation. His mental state improved significantly and he was admitted to the psychiatric ward. There he became increasingly disoriented, intermittently lethargic, febrile to 39°C (102°F) and was therefore transferred to the intensive care unit 20 hours after the initial emergency department presentation.

Due to phencyclidine intoxication and evidence of injury (multiple abrasions), rhabdomyolysis was considered. Extracellular volume expansion with a solution of 5% dextrose and 0.45% sodium chloride was initiated. A creatine kinase value of 46,000 units per liter confirmed muscle damage. Activated charcoal, 50 grams in 240 ml of 70% sorbitol (Actidose), was given through a nasogastric tube every four hours. Thirteen hours after medical transfer and two hours after his third dose of charcoal-sorbitol, his serum sodium concentration had increased to 165 mmol per liter, urine output had decreased to 50 ml per hour and a urine specific gravity was 1.029 (Figure 1). His blood pressure decreased from 130/65 mm of mercury (when admitted to the intensive care unit) to 110/50 mm of mercury, and urine electrolyte determinations showed a sodium of 29 and a potassium of 45 mmol per liter. During the previous eight hours, nurses had noticed several large and loose charcoal bowel movements. Water replacement with intravenous fluids returned the sodium concentrations to normal ranges over the next 20 hours, accompanied by increasing urine output and a decreasing urine specific gravity (Figure 1). The patient's mental state improved. After a seven-day stay on the medical floor, he was transferred back to the psychiatric unit because of bizarre behavior and suicidal ideas.

Discussion

Hypernatremia in adults is generally a chronic process associated with other illnesses that limit fluid intake—such as an elderly patient with a cerebrovascular accident. Acute hypernatremia has most commonly occurred due to solute loading—saline abortion, the use of sodium chloride as an emetic, malfunctioning hemodialysis or peritoneal dialysis equipment or sodium bicarbonate administration during a cardiac arrest.¹²

In each of the cases presented, the history and clinical evidence exclude the commonly recognized causes. Dilute sodium-containing fluids were administered at normal maintenance or replacement rates of infusion. Urinary water losses indicated appropriate volumes and specific gravities for the clinical volume states present. In case 2, fever and tachypnea may have exaggerated losses of water from the skin and respiratory tract but are unlikely to account for the entire deficit, considering a controlled environment and humidified air. Osmotic diuresis from hyperglycemia is also unlikely as the initial blood glucose level was 140 mg per dl and urine output remained low. Acute colonic water loss due to the osmotic or

saline cathartics administered remains the most likely cause of acute hypernatremia. In all three cases, nursing notes specifically document excessively loose and watery stools. In case 2, stools were occurring in frequencies too numerous to count. In case 1, the patient inadvertently received six doses of Actidose (a solution of 50 grams activated charcoal in 240 ml of 70% sorbitol) plus 300 ml of magnesium citrate solution over a period of 24 hours. The sorbitol vehicle was not specified on the front label of the Actidose preparation. Sorbitol is classified as a pharmaceutical aide¹³ and an inactive ingredient¹⁴ by the Food and Drug Administration.

Sorbitol is a hexahydric alcohol that is primarily used as a sweetener in diabetic diets and some low-calorie beverages. It has been used medicinally as a laxative and to facilitate the passage of sodium polystyrene sulfonate (Kayexalate) through the intestinal tract. The addition of 70% sorbitol as a vehicle for activated charcoal overcomes its grittiness, improves palatability, maintains particles in suspension for prolonged periods of time and provides a cathartic action.⁸

Several authors identify possible fluid and electrolyte losses due to the use of sorbitol. Diarrhea and electrolyte changes have been noted in children taking a vitamin C preparation containing sorbitol.² Minocha and associates studied the effects of a single dose of 30 grams of activated charcoal in 150 ml of 70% sorbitol on serum osmolarity, electrolytes, metabolic profile, magnesium level, hepatic enzymes and complete blood count in healthy adults.¹¹ They noted only small changes in serum sodium and phosphorus concentrations four hours after drinking the charcoal-sorbitol mixture, but recommended that the possible effects of multiple-dose regimens and the effects in pediatric and geriatric populations required further study. Krenzelok and colleagues in a single-dose study in volunteers examined the gastrointestinal transit times following three separately administered cathartics combined with 50 grams of activated charcoal—130 grams of 70% sorbitol, 300 ml of magnesium citrate solution and 30 ml of 50% magnesium sulfate.¹⁵ Sorbitol was clearly the most rapidly acting cathartic, producing a charcoal-colored stool in a mean time of 1.6 hours compared with 4.2 hours for magnesium citrate and 9.3 hours for magnesium sulfate. In the sorbitol group, some patients reported a frequency of 10 to 15 watery stools and complained of more abdominal cramping before catharsis. The authors warned that physicians should be aware of the potential for fluid and electrolyte depletion if sorbitol is used with each dose of activated charcoal in a multidose regimen.

Despite the demonstrated potency of sorbitol in these doses, its pharmaceutical classification allows commercial products to be sold over the counter without package insert information.

The outcome in two of our cases was uneventful following the correction of water losses. As described in case 2, however, the patient died of complications of the overdose and supportive management.

Conclusions

The safety and efficacy of repeated cathartic administration have not been established. Overdosed patients who may have ingested several drugs affecting bowel function may be at risk for rapid shifts of water and electrolytes into the bowel due to multiple doses of saline or osmotic cathartics. We recommend that administration of such cathartics should be limited to one or two doses per 24-hour period in children and

adults until further study defines the risks and benefits of this practice. We also suggest reconsideration of labeling guidelines for sorbitol-containing products formulated for pharmacologic effects.

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Rhabdomyosarcoma of the Heart with Cerebral Metastases

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RHABDOMYOSARCOMA OF THE HEART is a malignant neoplasm composed of cells that display features of striated muscle. This tumor is rare and accounts for less than 5% of all tumors and cysts of the heart and pericardium.¹ Cardiac rhabdomyosarcomas may occur in any of the four chambers of the heart, but a portion of the tumor always involves the myocardium, even when the intracavitary component predominates.¹ The clinical findings are determined by the anatomic location of the tumor and the degree of intracavitary obstruction.² The presenting features include congestive heart failure, precordial pain, pericardial effusion, conduction abnormalities, obstruction of the vena cava and sudden death.² Surgical treatment is usually not effective against cardiac rhabdomyosarcomas because of the extent of myocardial involvement or the presence of metastases. Because the tumor is rare, most reports consist of a single case or only a few cases and, thus, there are limited descriptions of the sites of metastases from this tumor.

A computer-assisted literature search elicited only one

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case³ of cerebral metastases from cardiac rhabdomyosarcoma. In this report I describe the second case of cerebral involvement by this unusual neoplasm and the first case reported in the English language literature.

Report of a Case

The patient, a 23-year-old man, had the sudden development of a cough productive of brown sputum. He had a systolic murmur and a pericardial friction rub. On radiographic examination there were bilateral pulmonary infiltrates, and a diagnosis of *Mycoplasma pneumoniae* was made. He did well, with resolution of the pneumonia, but one month later pulmonary edema developed. He had a high-pitched, heaving systolic and diastolic murmur.

A chest radiograph showed increased size of the left atrium, and an electrocardiogram revealed sinus tachycardia with nonspecific ST-T changes. An echocardiogram showed a mass in the left atrium, and cardiac catheterization revealed that the mass in the left atrium extended through the mitral valve. The patient underwent right and left atriectomies and atrioseptostomy for resection of the tumor. The tumor arose from the posterior wall of the left atrium. The surgical specimen showed rhabdomyosarcoma, and the margins of the specimen were free of tumor. The resected tumor was 10 by 8 by 6 cm and had a firm, white, fleshy appearance with areas of hemorrhage and necrosis. On microscopic examination of the primary tumor there was a neoplastic proliferation of cells with abundant eosinophilic cytoplasm and large, hyperchromatic nuclei displaying numerous mitoses. Cross-striations characteristic of skeletal muscle differentiation were found in the tumor cells (Figure 1).

The patient did well postoperatively, was evaluated for metastases and found to be free of tumor. He received chemotherapy consisting of cyclophosphamide (Cytosan), 200 mg, and vincristine sulfate, 2 mg, intravenously per week for 12 weeks and dactinomycin, 0.5 grams, intravenously for 5 days every 3 months. After the 11th postoperative week, the vincristine therapy was discontinued because of tingling in the patient's hands. He received the other chemotherapy without apparent toxicity.

Six months later the patient had throbbing pain in the left pectoral region, shoulder and upper arms. He was admitted to hospital where a workup included a bone scan and multigate analysis (MUGA) scans, which were normal. He continued to

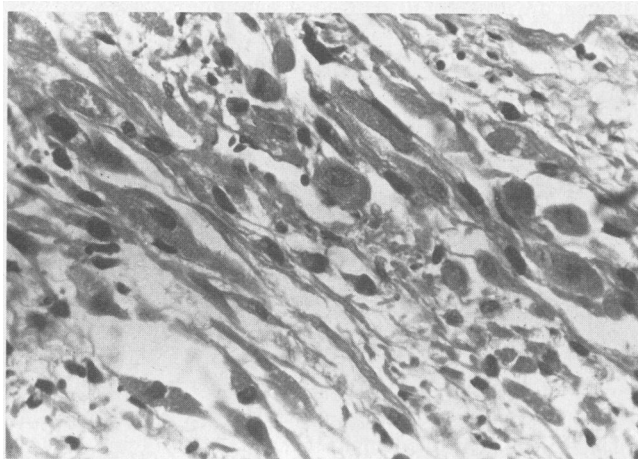


Figure 1.—Tumor cells from the occipital mass contain cross-striations, which identify the tumor as a rhabdomyosarcoma (Hand E, original magnification $\times 450$).